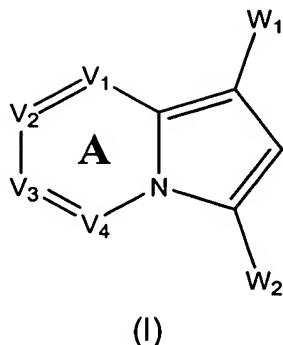
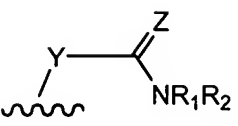
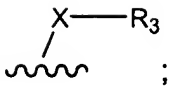


WE CLAIM:

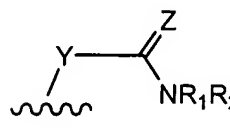
1. A compound of Formula (I):



wherein:

one of W_1 and W_2 is  and the other is  ;

V_1 , V_2 , V_3 and V_4 are independently CR_6 or N; or alternatively, V_1 and V_2 taken together or V_3 and V_4 taken together may be replaced with S, O, or NR_7 to form a fused 5-membered heterocyclic ring, and wherein two adjacent positions on Ring A may optionally be joined to create a fused aryl group, provided that when W_1 is

, V_1 , V_2 , V_3 and V_4 may not all be CR_6 ;

X is a covalent bond, $-C(R_4R_5)-$, $-N(R_4)-$, $-O-$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-C(=O)-$, $-C(=O)-N(R_4)-$, or $-N(R_4)-C(=O)-$;

Y is $-C(R_4R_5)-$, $-N(R_4)-$, $-O-$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-C(=O)-$, $-C(=S)-$, $-C(=O)-N(R_4)-$, $-C(=N-OR_8)-$, $-C(=N-R_8)-$, or $-N(R_4)-C(=O)-$;

Z is $=O$, $=S$, $=N-OR_8$ or $=NR_8$;

R_1 and R_2 are independently -H, an unsubstituted aliphatic group, a substituted aliphatic group, an unsubstituted non-aromatic heterocyclic group, a substituted non-aromatic heterocyclic group, an unsubstituted aryl group or a substituted aryl group, or alternatively, NR_1R_2 , taken together, is a substituted or unsubstituted non-aromatic nitrogen-containing heterocyclic group or a substituted or unsubstituted nitrogen-containing heteroaryl group;

R₃ is a substituted or unsubstituted aryl group or a substituted or unsubstituted aliphatic group;

each R₄ and R₅ is independently -H or a substituted or unsubstituted aliphatic group;

each R₆ is independently -H or a Ring A substituent;

each R₇ is independently -H or a heteroaryl ring nitrogen substituent and

each R₈ is independently -H, an unsubstituted aliphatic group, a substituted aliphatic group, an unsubstituted non-aromatic heterocyclic group, a substituted non-aromatic heterocyclic group, an unsubstituted aryl group, or a substituted aryl group; and pharmaceutically acceptable salts and prodrugs thereof.

2. The compound according to claim 1, wherein

X is -C(R₄R₅)-, -N(R₄)-, -C(=O)- or -O-;

Y is -C(R₄R₅)- or C=O;

Z is =O;

R₁ is -H;

R₂ is a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group;

R₃ is a substituted or unsubstituted aryl group;

R₆ is independently selected from H, halo, -C₁-C₄ alkyl, -C₁-C₄ alkoxy, -C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, -C₁-C₄ acyl, amido, substituted amido, -NO₂, -CN, -OH, -NH₂ and substituted amino; and

each R₈ is independently -H or a substituted or unsubstituted aliphatic group.

3. The compound according to claim 2, wherein:

X is -CH₂-, -CH(lower alkyl)-, -NH-, -N(lower alkyl)-, -C(=O)- or -O-;

Y is C=O;

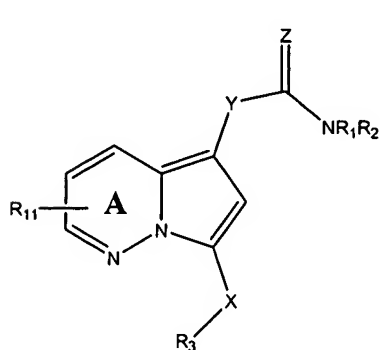
R₂ is an unsubstituted aryl group or an aryl group substituted with lower alkyl, amido, cyano or halo;

R₃ is a substituted or unsubstituted phenyl, pyridyl or thienyl group;

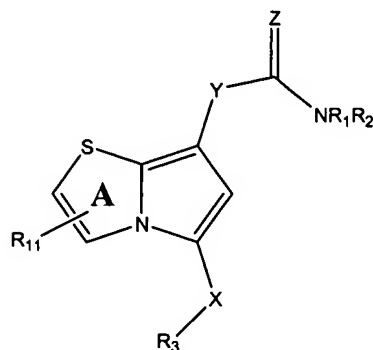
R₄ and R₅ are both H; and

each R_8 is independently $-H$ or a substituted or unsubstituted lower alkyl.

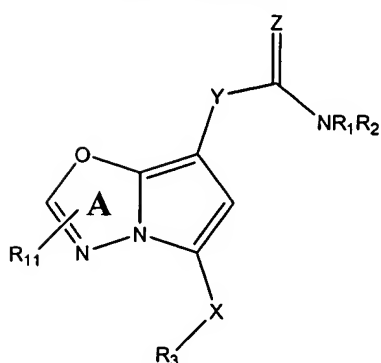
4. The compound according to claim 1, having the structure of Formula (Ia), (Ib), (Ic), (Id), (Ie), (If) or (Ig):



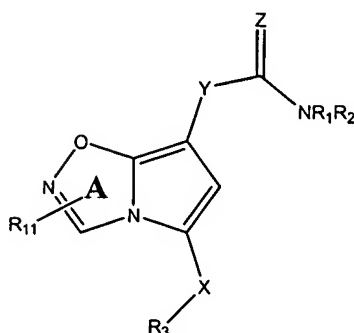
Formula (Ia)



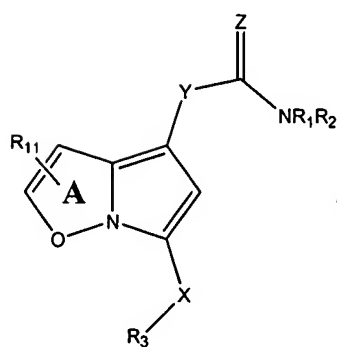
Formula (Ib)



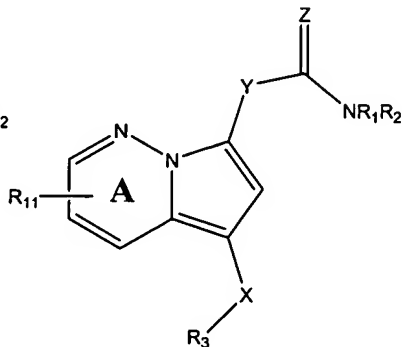
Formula (Ic)



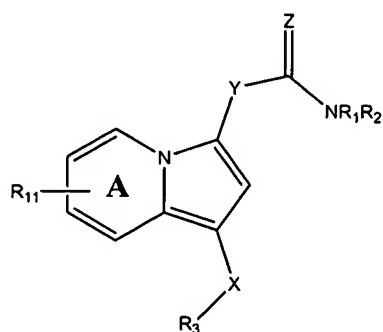
Formula (Id)



Formula (Ie)



Formula (If)



Formula (Ig)

wherein X is a covalent bond, $-C(R_4R_5)-$, $-N(R_4)-$, $-O-$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-C(=O)-$, $-C(=O)-N(R_4)-$, or $-N(R_4)-C(=O)-$;

Y is -C(R₄R₅)-, -N(R₄)-, -O-, -S-, -S(O)-, -S(O)₂-, -C(=O)-, -C(=S)-, -C(=O)-N(R₄)-, -C(=N-OR₈)-, -C(=N-R₈)-, or -N(R₄)-C(=O)-;

Z is =O, =S, =N-OR₈ or =NR₈;

R₁ and R₂ are independently -H, an unsubstituted aliphatic group, a substituted aliphatic group, an unsubstituted non-aromatic heterocyclic group, a substituted non-aromatic heterocyclic group, an unsubstituted aryl group or a substituted aryl group; or alternatively, NR₁R₂, taken together, is a substituted or unsubstituted non-aromatic nitrogen-containing heterocyclic group or a substituted or unsubstituted nitrogen-containing heteroaryl group;

R₃ is a substituted or unsubstituted aryl group or a substituted or unsubstituted aliphatic group;

each R₄ and R₅ is independently -H or a substituted or unsubstituted aliphatic group;

each R₈ is independently -H, an unsubstituted aliphatic group, a substituted aliphatic group, an unsubstituted non-aromatic heterocyclic group, a substituted non-aromatic heterocyclic group, an unsubstituted aryl group, or a substituted aryl group;

each R₁₁ is independently selected from Ring A substituents (preferably, selected from the group consisting of H, hydroxyl, cyano, nitro, halo, a substituted or unsubstituted amino group, a substituted or unsubstituted acyl group, a substituted or unsubstituted amido group, a substituted or unsubstituted alkyl group, a substituted or unsubstituted alkoxy group, or a substituted or unsubstituted aryl group; and

pharmaceutically acceptable salts and prodrugs thereof.

5. The compound according to claim 4, wherein

X is -C(R₄R₅)-, -N(R₄)-, -C(=O)- or -O-;

Y is -C(R₄R₅)- or C=O;

Z is =O;

R₁ is -H;

R₂ is a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group;

R₃ is a substituted or unsubstituted aryl group; and

each R_8 is independently $-H$ or a substituted or unsubstituted aliphatic group.

6. The compound according to claim 3, wherein:

X is $-CH_2-$, $-CH(\text{lower alkyl})-$, $-NH-$, $-N(\text{lower alkyl})-$, $-C(=O)-$ or $-O-$;

Y is $C=O$;

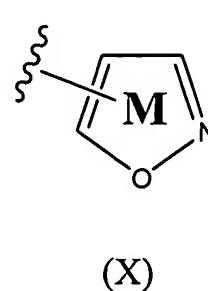
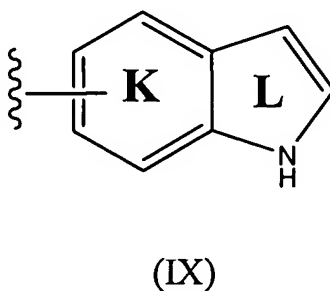
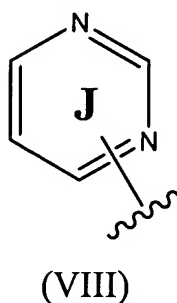
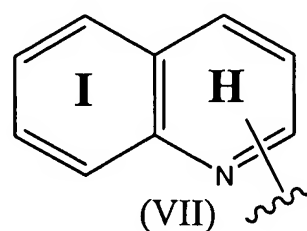
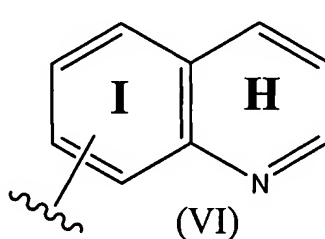
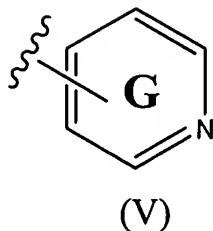
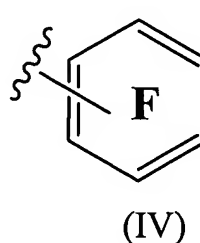
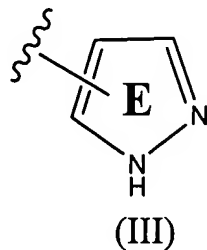
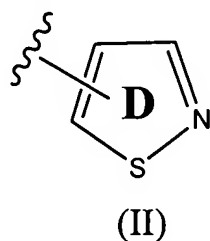
R_2 is an unsubstituted aryl group or an aryl group substituted with lower alkyl, amido, cyano or halo;

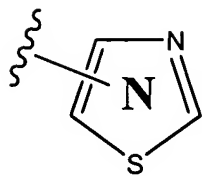
R_3 is a substituted or unsubstituted phenyl, pyridyl or thienyl group;

R_4 and R_5 are both H; and

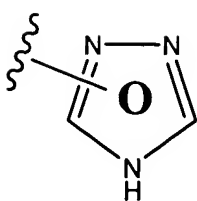
each R_8 is independently $-H$ or a substituted or unsubstituted lower alkyl.

7. The compound according to claim 1, wherein R_2 is selected from the group consisting of Formulas (II)-(XV):

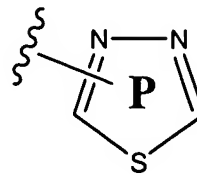




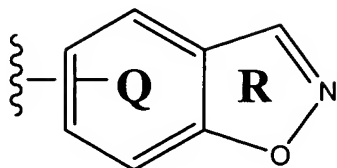
(XI)



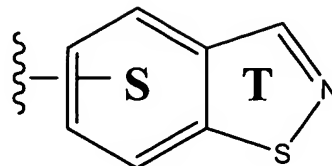
(XII)



(XIII)



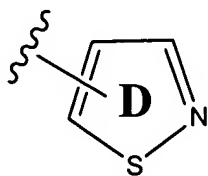
(XIV)



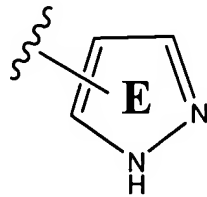
(XV)

wherein each of rings Rings **D-T** may be substituted or unsubstituted.

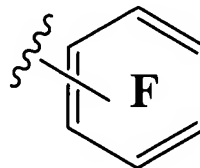
8. The compound according to claim 4, wherein R_2 is selected from the group consisting of Formulas (II)-(XV):



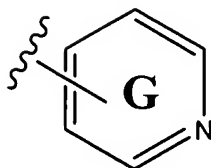
(II)



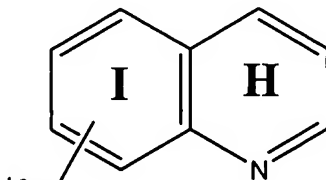
(III)



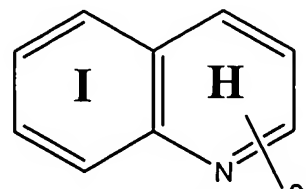
(IV)



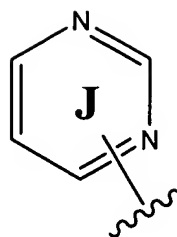
(V)



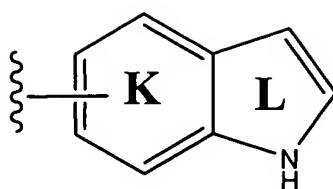
(VI)



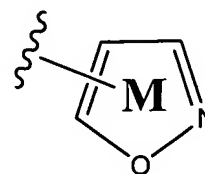
(VII)



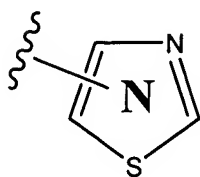
(VIII)



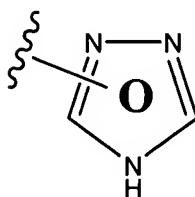
(IX)



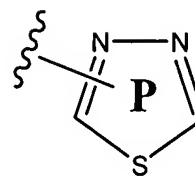
(X)



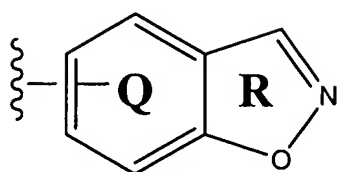
(XI)



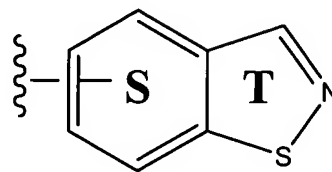
(XII)



(XIII)



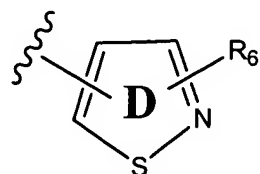
(XIV)



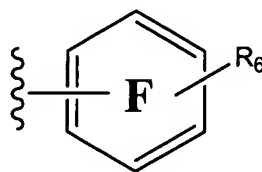
(XV)

wherein each of rings Rings **D-T** may be substituted or unsubstituted.

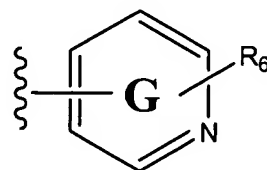
9. The compound according to claim 7, wherein R_2 is selected from Formulas (XVI)-(XXI):



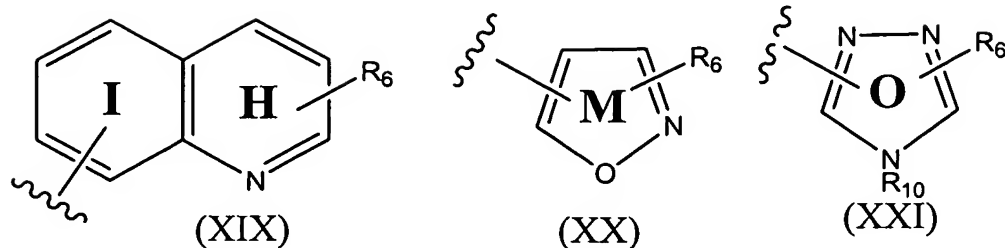
(XVI)



(XVII)



(XVIII)

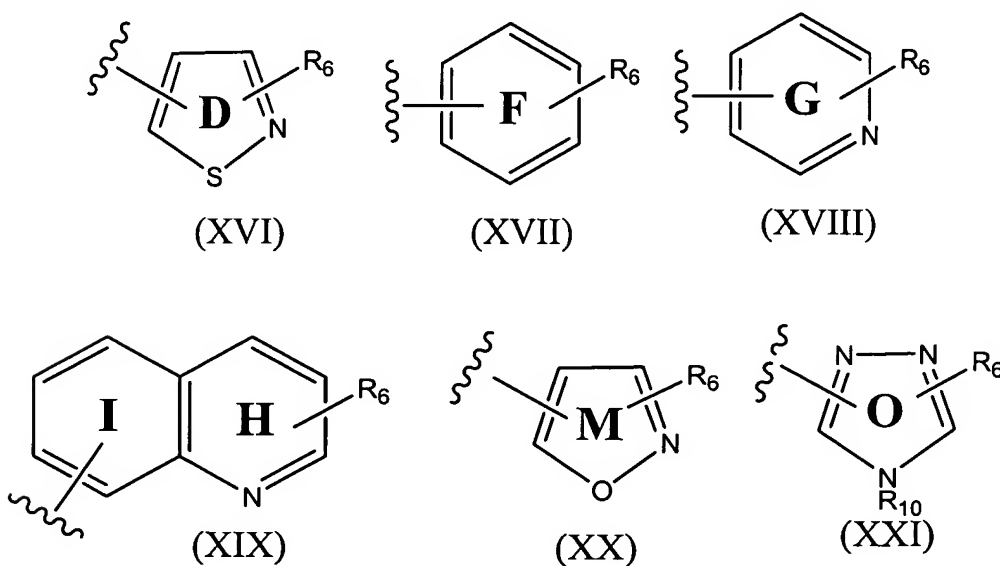


wherein

each R₆ is independently selected from the group consisting of H, hydroxyl, cyano, nitro, halo, a substituted or unsubstituted alkyl group, a substituted or unsubstituted alkoxy group, or a substituted or unsubstituted aryl group; and

R₁₀ is -H or a substituted or unsubstituted alkyl group.

10. The compound according to claim 8, wherein R₂ is selected from Formulas (XVI)-(XXI):

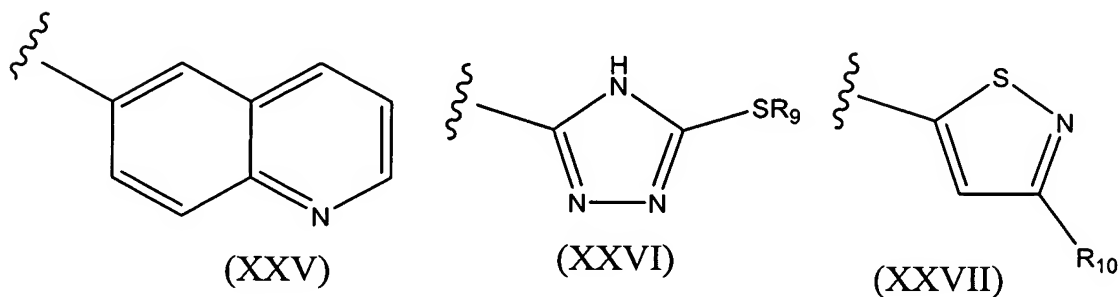
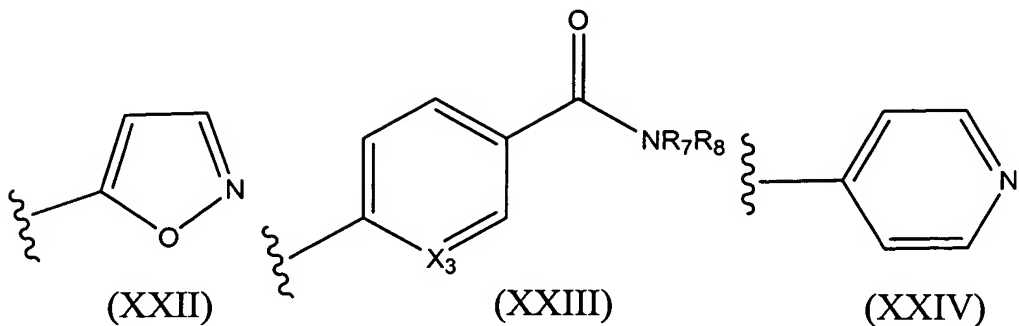


wherein

each R₆ is independently selected from the group consisting of H, hydroxyl, cyano, nitro, halo, a substituted or unsubstituted alkyl group, a substituted or unsubstituted alkoxy group, or a substituted or unsubstituted aryl group; and

R₁₀ is -H or a substituted or unsubstituted alkyl group.

11. The compound according to claim 9, wherein R_2 is selected from Formulas (XXII)-(XXVII):



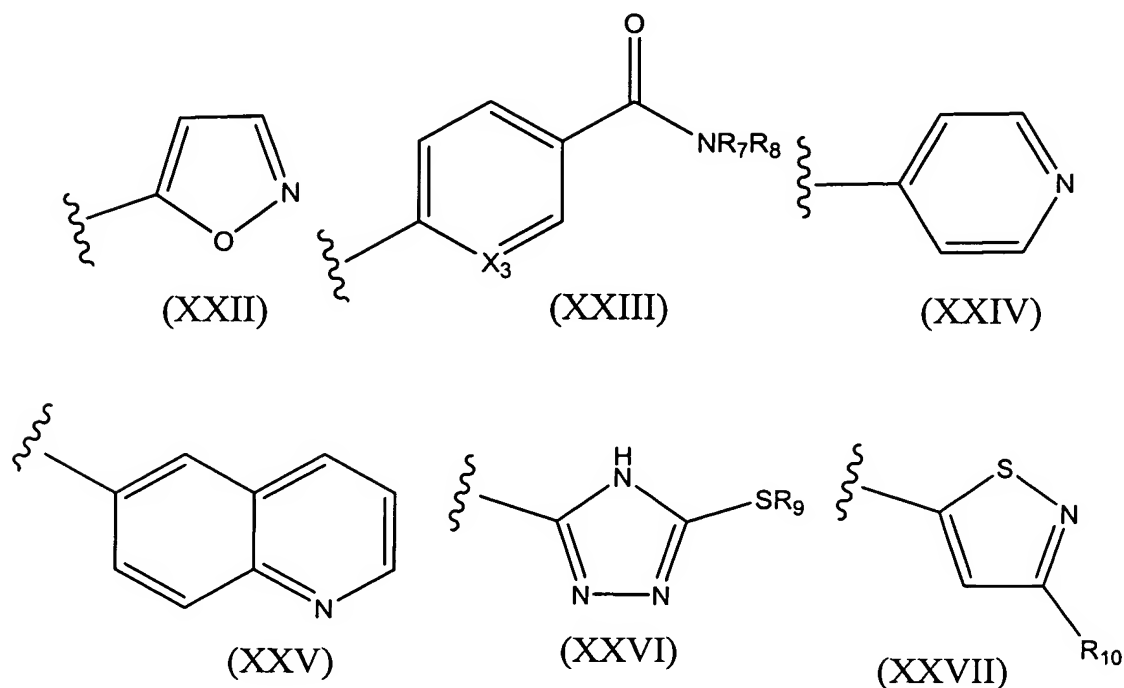
wherein X_3 is -CH- or -N-;

R_7 and R_8 are independently -H or an alkyl group or alternatively, - NR_7R_8 , taken together, is a nitrogen-containing non-aromatic heterocyclic group;

R_9 is an alkyl group; and

R_{10} is -H or an alkyl group.

12. The compound according to claim 10, wherein R_2 is selected from Formulas (XXII)-(XXVII):



wherein X_3 is -CH- or -N-;

R_7 and R_8 are independently -H or an alkyl group or alternatively, $-NR_7R_8$, taken together, is a nitrogen-containing non-aromatic heterocyclic group;

R_9 is an alkyl group; and

R_{10} is -H or an alkyl group.

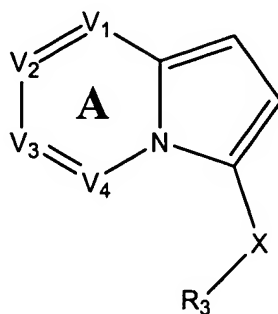
13. A compound selected from the group consisting of Compounds (I-1) through (I-14).

14. A pharmaceutical composition comprising at least one compound according to claim 1 and a pharmaceutically acceptable carrier.

15. The pharmaceutical composition of claim 14, further comprising one or more additional therapeutic agents.

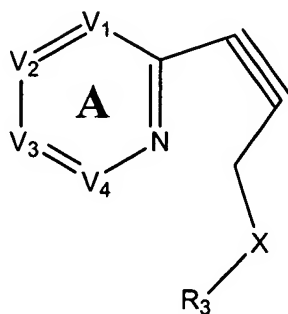
16. The pharmaceutical composition of claim 15, wherein the additional therapeutic agent is an agent against cancer agent, an autoimmune disease, an inflammatory disorder or pain.
17. A method for treating cancer, an inflammatory disorder or an autoimmune disease comprising the step of administering to a subject in need thereof an effective amount of the pharmaceutical composition according to claim 14.
18. A method for preventing cancer, an inflammatory disorder or an autoimmune disease comprising the step of administering to a subject in need thereof an effective amount of the pharmaceutical composition according to claim 14.
19. A method for preventing or treating a disorder involving PDE4 or elevated levels of cytokines comprising the step of administering to a subject in need thereof an effective amount of the pharmaceutical composition according to claim 14.
20. The method according to claim 19, wherein the disorder is characterized, mediated or exacerbated by overproduction or activity of $\text{TNF}\alpha$.
21. The method according to claim 19, wherein the disorder is characterized, mediated or exacerbated by overproduction or activity of PDE4.
22. A method of inhibiting $\text{TNF}\alpha$ or PDE4 in a cell comprising the step of contacting the cell with an effective amount of a compound according to claim 1.
23. A method for reducing $\text{TNF}\alpha$ levels in a subject comprising administering to the subject an effective amount of a compound according to claim 1.
24. A method for suppressing inflammatory cell activation comprising the step of contacting the cell with an effective amount of a compound according to claim 1.

25.A method of preparing a compound of Formula (I_{INT-A}):



(I_{INT-A})

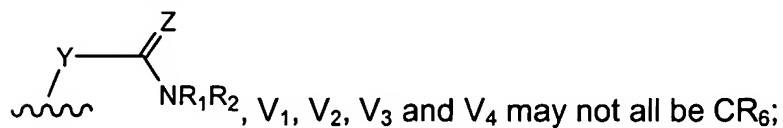
comprising the step of reacting a Cu^I salt with a precursor compound represented by Formula (I_{INT-B}):



(I_{INT-B})

wherein

V₁, V₂, V₃ and V₄ are independently CR₆ or N; or alternatively, V₁ and V₂ taken together or V₃ and V₄ taken together may be replaced with S, O, or NR₇ to form a fused 5-membered heterocyclic ring, and wherein two adjacent positions on Ring A may optionally be joined to create a fused aryl group, provided that when W₁ is



X is a covalent bond, -C(R₄R₅)-, -N(R₄)-, -O-, -S-, -S(O)-, -S(O)₂-, -C(=O)-, -C(=O)-N(R₄)-, or -N(R₄)-C(=O)-;

Y is $-C(R_4R_5)-$, $-N(R_4)-$, $-O-$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-C(=O)-$, $-C(=S)-$, $-C(=O)-N(R_4)-$, $-C(=N-OR_8)-$, $-C(=N-R_8)-$, or $-N(R_4)-C(=O)-$;

Z is $=O$, $=S$, $=N-OR_8$ or $=NR_8$;

R_1 and R_2 are independently $-H$, an unsubstituted aliphatic group, a substituted aliphatic group, an unsubstituted non-aromatic heterocyclic group, a substituted non-aromatic heterocyclic group, an unsubstituted aryl group or a substituted aryl group; or alternatively, NR_1R_2 , taken together, is a substituted or unsubstituted non-aromatic nitrogen-containing heterocyclic group or a substituted or unsubstituted nitrogen-containing heteroaryl group;

R_3 is a substituted or unsubstituted aryl group or a substituted or unsubstituted aliphatic group, provided that R_3 is not a substituted or unsubstituted alkyl group;

each R_4 and R_5 is independently $-H$ or a substituted or unsubstituted aliphatic group;

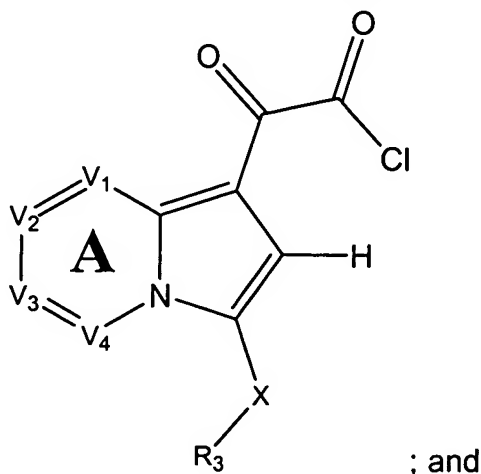
each R_6 is independently $-H$ or a Ring **A** substituent;

each R_7 is independently $-H$ or a heteroaryl ring nitrogen substituent; and

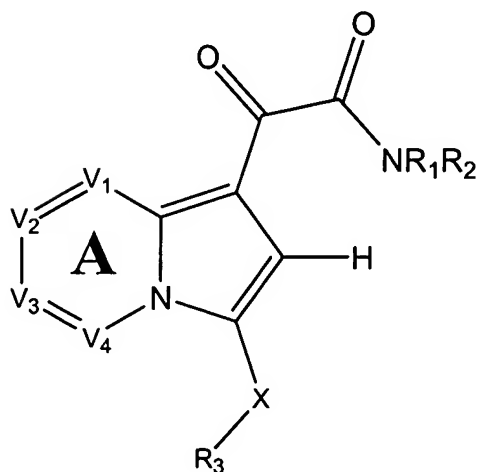
each R_8 is independently $-H$, an unsubstituted aliphatic group, a substituted aliphatic group, an unsubstituted non-aromatic heterocyclic group, a substituted non-aromatic heterocyclic group, an unsubstituted aryl group, or a substituted aryl group.

26. The method of claim 25, further comprising the steps of:

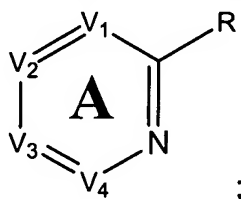
- a) reacting the compound of Formula (I_{INT-A}) with oxalyl chloride to form a product compound represented by the following structural formula:



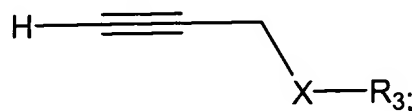
- b) amidating the product compound with NHR_1R_2 to form a second product compound represented by the following formula:



27. The method of Claim 25, wherein the compound of Formula (I_{INT-B}) is prepared by reacting a pyridine starting compound and an alkyne starting material in the presence of a catalytic amount of a palladium^{II} salt and a Cu^I salt, wherein the starting compound is represented by the following structural formula:

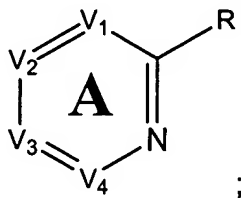


the alkyne starting material is represented by the following structural formula:

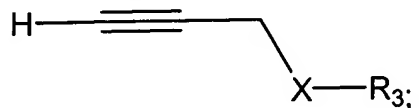


and R is -Br or -I.

28. The method of Claim 26, wherein the compound of Formula (I_{INT-B}) is prepared by reacting a pyridine starting compound and an alkyne starting material in the presence of a catalytic amount of a palladium^{II} salt and a Cu^I salt, wherein the starting compound is represented by the following structural formula:



the alkyne starting material is represented by the following structural formula:



and R is -Br or -I.